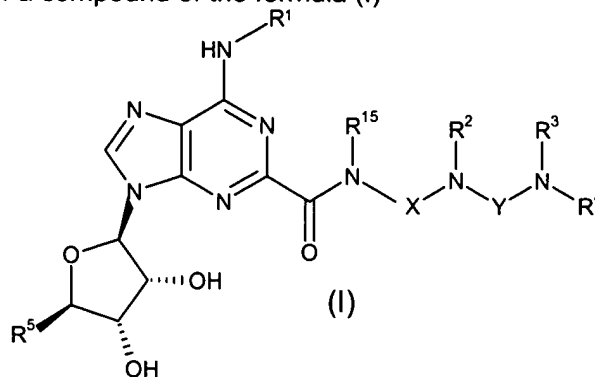


- Amendments to the Claims -

1. - 57. (Canceled)

58. (Currently amended) A method of treatment of a mammal, including a human being, to treat an inflammatory disease including treating said mammal with an effective amount of a compound of the formula (I)



or a pharmaceutically acceptable salt or solvate thereof, wherein
R¹ is H, C₁-C₆ alkyl or fluorenyl, said C₁-C₆ alkyl being optionally substituted by 1 or 2 substituents each independently selected from phenyl and naphthyl, said phenyl and naphthyl being optionally substituted by C₁-C₆ alkyl, C₁-C₆ alkoxy, halo or cyano;
(A) R² is H or C₁-C₆ alkyl, R¹⁵ is H or C₁-C₆ alkyl, and X is either (i) unbranched C₂-C₃ alkylene optionally substituted by C₁-C₆ alkyl or C₃-C₈ cycloalkyl, or (ii) a group of the formula:



where W is C₅-C₇ cycloalkylene optionally substituted by C₁-C₆ alkyl, n is 0 or 1 and p is 0 or 1, or

(B) R¹⁵ is H or C₁-C₆ alkyl, and R² and X, taken together with the nitrogen atom to which they are attached, represent azetidin-3-yl, pyrrolidin-3-yl, piperidin-3-yl, piperidin-4-yl, homopiperidin-3-yl or homopiperidin-4-yl, each being optionally substituted by C₁-C₆ alkyl, or

(C) R² is H or C₁-C₆ alkyl, and R¹⁵ and X, taken together with the nitrogen atom to which they are attached, represent azetidin-3-yl, pyrrolidin-3-yl, piperidin-3-yl, piperidin-4-yl, homopiperidin-3-yl or homopiperidin-4-yl, each being optionally substituted by C₁-C₆ alkyl;

either, R³ and R⁴, taken together with the nitrogen atom to which they are attached, represent azetidiny, pyrrolidinyl, piperidinyl, piperazinyl, homopiperidinyl or homopiperazinyl, each being optionally substituted on a ring nitrogen or carbon atom by C₁-C₆ alkyl or C₃-C₈ cycloalkyl and optionally substituted on a ring carbon atom not adjacent to a ring nitrogen atom by -NR⁶R⁷,

or, R³ is H, C₁-C₆ alkyl, C₃-C₈ cycloalkyl or benzyl and R⁴ is

(a) azetidin-3-yl, pyrrolidin-3-yl, piperidin-3-yl, piperidin-4-yl, homopiperidin-3-yl or homopiperidin-4-yl, each being optionally substituted by C₁-C₆ alkyl, C₃-C₈ cycloalkyl, phenyl, benzyl or het, or

(b) -(C₂-C₆ alkylene)-R⁸

(c) -(C₁-C₆ alkylene)-R¹³, or

(d) C₁-C₆ alkyl or C₃-C₈ cycloalkyl;

R⁵ is CH₂OH or CONR¹⁴R¹⁴;

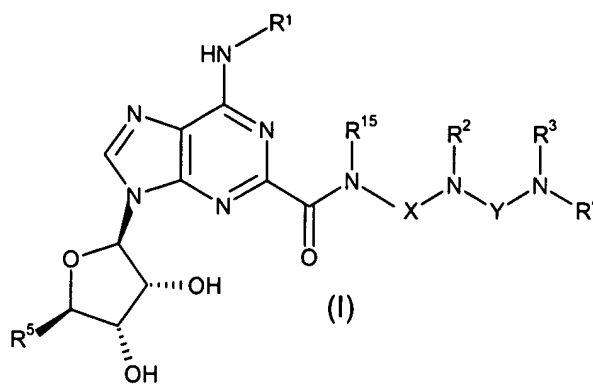
R⁶ and R⁷ are either each independently H or C₁-C₆ alkyl or, taken together with the nitrogen atom to which they are attached, represent azetidiny, pyrrolidinyl or

piperidinyl, said azetidiny, pyrrolidinyl and piperidinyl being optionally substituted by C₁-C₆ alkyl;
R⁸ is (i) azetidin-1-yl, pyrrolidin-1-yl, piperidin-1-yl, morpholin-4-yl, piperazin-1-yl, homopiperidin-1-yl, homopiperazin-1-yl or tetrahydroisoquinolin-1-yl, each being optionally substituted on a ring carbon atom by C₁-C₆ alkyl, C₃-C₈ cycloalkyl, phenyl, C₁-C₆ alkoxy-(C₁-C₆)-alkyl, R⁹R⁹N-(C₁-C₆)-alkyl, fluoro-(C₁-C₆)-alkyl, -CONR⁹R⁹, -COOR⁹ or C₂-C₅ alkanoyl, and optionally substituted on a ring carbon atom not adjacent to a ring nitrogen atom by fluoro-(C₁-C₆)-alkoxy, halo, -OR⁹, cyano, -S(O)_mR¹⁰, -NR⁹R⁹, -SO₂NR⁹R⁹, -NR⁹COR¹⁰ or -NR⁹SO₂R¹⁰, and said piperazin-1-yl and homopiperazin-1-yl being optionally substituted on the ring nitrogen atom not attached to the C₂-C₆ alkylene group by C₁-C₆ alkyl, phenyl, C₁-C₆ alkoxy-(C₂-C₆)-alkyl, R⁹R⁹N-(C₂-C₆)-alkyl, fluoro-(C₁-C₆)-alkyl, C₂-C₅ alkanoyl, -COOR¹⁰, C₃-C₈ cycloalkyl, -SO₂R¹⁰, -SO₂NR⁹R⁹ or -CONR⁹R⁹, or
(ii) NR¹¹R¹²;
R⁹ is H, C₁-C₆ alkyl, C₃-C₈ cycloalkyl or phenyl;
R¹⁰ is C₁-C₆ alkyl, C₃-C₈ cycloalkyl or phenyl;
R¹¹ is H, C₁-C₆ alkyl, C₃-C₈ cycloalkyl or benzyl;
R¹² is H, C₁-C₆ alkyl, C₃-C₈ cycloalkyl, phenyl, benzyl, fluoro-(C₁-C₆)-alkyl, -CONR⁹R⁹, -COOR¹⁰, C₂-C₅ alkanoyl or -SO₂NR⁹R⁹;
R¹³ is (a) phenyl, pyridin-2-yl, pyridin-3-yl or pyridin-4-yl, each being optionally substituted by C₁-C₆ alkyl, C₁-C₆ alkoxy, -(C₁-C₃ alkylene)-(C₁-C₆ alkoxy), halo, cyano, -(C₁-C₃ alkylene)-CN, -CO₂H, -(C₁-C₃ alkylene)-CO₂H, -CO₂(C₁-C₆ alkyl), -(C₁-C₃ alkylene)-CO₂(C₁-C₆ alkyl), -(C₁-C₃ alkylene)-NR¹⁴R¹⁴, -CONR¹⁴R¹⁴ or -(C₁-C₃ alkylene)-CONR¹⁴R¹⁴, or (b) azetidin-2-yl, azetidin-3-yl, pyrrolidin-2-yl, pyrrolidin-3-yl, piperidin-2-yl, piperidin-3-yl, piperidin-4-yl, homopiperidin-2-yl, homopiperidin-3-yl or homopiperidin-4-yl, each being optionally substituted by C₁-C₆ alkyl, C₃-C₈ cycloalkyl, phenyl, benzyl or het;
R¹⁴ is H or C₁-C₆ alkyl optionally substituted by cyclopropyl;
m is 0, 1 or 2;
Y is CO, CS, SO₂ or C=N(CN); and
"het", used in the definition of R⁴ and R¹³, is a C-linked, 4- to 6-membered ring, heterocycle having either from 1 to 4 ring nitrogen heteroatoms or 1 or 2 nitrogen ring heteroatoms and 1 oxygen or 1 sulphur ring heteroatom, optionally substituted by C₁-C₆ alkyl, C₃-C₈ cycloalkyl, C₁-C₆ alkoxy, C₃-C₈ cycloalkoxy, hydroxy, oxo or halo or with a pharmaceutically acceptable salt, solvate or composition thereof, as claimed in any one of claims 1 to 44 and 45 respectively.

59. (Canceled)

60. (Canceled)

61. (Original) A method of treatment of a mammal, including a human being, to treat septic shock, male erectile dysfunction, male factor infertility, female factor infertility, hypertension, stroke, epilepsy, cerebral ischaemia, peripheral vascular disease, post-ischaemic reperfusion injury, diabetes, rheumatoid arthritis, multiple sclerosis, psoriasis, dermatitis, allergic dermatitis, eczema, ulcerative colitis, Crohns disease, inflammatory bowel disease, *Helicobacter pylori* gastritis, non-*Helicobacter pylori* gastritis, non-steroidal anti-inflammatory drug-induced damage to the gastrointestinal tract or a psychotic disorder, or for wound healing, including treating said mammal with an effective amount of a compound of the formula (I)



or a pharmaceutically acceptable salt or solvate thereof, wherein

R¹ is H, C₁-C₆ alkyl or fluorenyl, said C₁-C₆ alkyl being optionally substituted by 1 or 2 substituents each independently selected from phenyl and naphthyl, said phenyl and naphthyl being optionally substituted by C₁-C₆ alkyl, C₁-C₆ alkoxy, halo or cyano;

(A) R² is H or C₁-C₆ alkyl, R¹⁵ is H or C₁-C₆ alkyl, and X is either (i) unbranched C₂-C₃ alkylene optionally substituted by C₁-C₆ alkyl or C₃-C₈ cycloalkyl, or (ii) a group of the formula:



where W is C₅-C₇ cycloalkylene optionally substituted by C₁-C₆ alkyl, n is 0 or 1 and p is 0 or 1, or

(B) R¹⁵ is H or C₁-C₆ alkyl, and R² and X, taken together with the nitrogen atom to which they are attached, represent azetidin-3-yl, pyrrolidin-3-yl, piperidin-3-yl, piperidin-4-yl, homopiperidin-3-yl or homopiperidin-4-yl, each being optionally substituted by C₁-C₆ alkyl, or

(C) R² is H or C₁-C₆ alkyl, and R¹⁵ and X, taken together with the nitrogen atom to which they are attached, represent azetidin-3-yl, pyrrolidin-3-yl, piperidin-3-yl, piperidin-4-yl, homopiperidin-3-yl or homopiperidin-4-yl, each being optionally substituted by C₁-C₆ alkyl;

either, R³ and R⁴, taken together with the nitrogen atom to which they are attached, represent azetidiny, pyrrolidinyl, piperidinyl, piperazinyl, homopiperidinyl or homopiperazinyl, each being optionally substituted on a ring nitrogen or carbon atom by C₁-C₆ alkyl or C₃-C₈ cycloalkyl and optionally substituted on a ring carbon atom not adjacent to a ring nitrogen atom by -NR⁶R⁷,

or, R³ is H, C₁-C₆ alkyl, C₃-C₈ cycloalkyl or benzyl and R⁴ is

(a) azetidin-3-yl, pyrrolidin-3-yl, piperidin-3-yl, piperidin-4-yl, homopiperidin-3-yl or homopiperidin-4-yl, each being optionally substituted by C₁-C₆ alkyl, C₃-C₈ cycloalkyl, phenyl, benzyl or het, or

(b) -(C₂-C₆ alkylene)-R⁸

(c) -(C₁-C₆ alkylene)-R¹³, or

(d) C₁-C₆ alkyl or C₃-C₈ cycloalkyl;

R⁹ is CH₂OH or CONR¹⁴R¹⁴.

R⁶ and R⁷ are either each independently H or C₁-C₆ alkyl or, taken together with the nitrogen atom to which they are attached, represent azetidiny, pyrrolidinyl or piperidinyl, said azetidiny, pyrrolidinyl and piperidinyl being optionally substituted by C₁-C₆ alkyl;

R⁸ is (i) azetidin-1-yl, pyrrolidin-1-yl, piperidin-1-yl, morpholin-4-yl, piperazin-1-yl, homopiperidin-1-yl, homopiperazin-1-yl or tetrahydroisoguinolin-1-yl, each being optionally substituted on a ring carbon atom by C₁-C₆ alkyl, C₃-C₈ cycloalkyl, phenyl, C₁-C₆ alkoxy-(C₁-C₆)-alkyl, R⁹R⁹N-(C₁-C₆)-alkyl, fluoro-(C₁-C₆)-alkyl, -CONR⁹R⁹, -COOR⁹ or C₂-C₅ alkanoyl, and optionally substituted on a ring carbon atom not adjacent to a ring nitrogen atom by fluoro-(C₁-C₆)-alkoxy, halo, -OR⁹, cyano, -S(O)_mR¹⁰,

-NR⁹R⁹, -SO₂NR⁹R⁹, -NR⁹COR¹⁰ or -NR⁹SO₂R¹⁰, and said piperazin-1-yl and homopiperazin-1-yl being optionally substituted on the ring nitrogen atom not attached to the C₂-C₆ alkylene group by C₁-C₆ alkyl, phenyl, C₁-C₆ alkoxy-(C₂-C₆)-alkyl, R⁹R⁹N-(C₂-C₆)-alkyl, fluoro-(C₁-C₆)-alkyl, C₂-C₅ alkanoyl, -COOR¹⁰, C₃-C₈ cycloalkyl, -SO₂R¹⁰, -SO₂NR⁹R⁹ or -CONR⁹R⁹, or

(ii) NR¹¹R¹²,

R⁹ is H, C₁-C₆ alkyl, C₃-C₈ cycloalkyl or phenyl;

R¹⁰ is C₁-C₆ alkyl, C₃-C₈ cycloalkyl or phenyl;

R¹¹ is H, C₁-C₆ alkyl, C₃-C₈ cycloalkyl or benzyl;

R¹² is H, C₁-C₆ alkyl, C₃-C₈ cycloalkyl, phenyl, benzyl, fluoro-(C₁-C₆)-alkyl, -CONR⁹R⁹, -COOR¹⁰, C₂-C₅ alkanoyl or -SO₂NR⁹R⁹;

R¹³ is (a) phenyl, pyridin-2-yl, pyridin-3-yl or pyridin-4-yl, each being optionally substituted by C₁-C₆ alkyl, C₁-C₆ alkoxy, -(C₁-C₃ alkylene)-(C₁-C₆ alkoxy), halo, cyano, -(C₁-C₃ alkylene)-CN, -CO₂H, -(C₁-C₃ alkylene)-CO₂H, -CO₂(C₁-C₆ alkyl), -(C₁-C₃ alkylene)-CO₂(C₁-C₆ alkyl), -(C₁-C₃ alkylene)-NR¹⁴R¹⁴, -CONR¹⁴R¹⁴ or -(C₁-C₃ alkylene)-CONR¹⁴R¹⁴, or (b) azetidin-2-yl, azetidin-3-yl, pyrrolidin-2-yl, pyrrolidin-3-yl, piperidin-2-yl, piperidin-3-yl, piperidin-4-yl, homopiperidin-2-yl, homopiperidin-3-yl or homopiperidin-4-yl, each being optionally substituted by C₁-C₆ alkyl, C₃-C₈ cycloalkyl, phenyl, benzyl or het;

R¹⁴ is H or C₁-C₆ alkyl optionally substituted by cyclopropyl;

m is 0, 1 or 2;

Y is CO, CS, SO₂ or C=N(CN); and

"het", used in the definition of R⁴ and R¹³, is a C-linked, 4- to 6-membered ring, heterocycle having either from 1 to 4 ring nitrogen heteroatoms or 1 or 2 nitrogen ring heteroatoms and 1 oxygen or 1 sulphur ring heteroatom, optionally substituted by C₁-C₆ alkyl, C₃-C₈ cycloalkyl, C₁-C₆ alkoxy, C₃-C₈ cycloalkoxy, hydroxy, oxo or halo or with a pharmaceutically acceptable salt, solvate or composition thereof, as claimed in any one of claims 1 to 44 and 45 respectively.

62. - 77. (Canceled)

An early and favorable action is respectfully requested.

Respectfully submitted,

Dated: October 1, 2003

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